SONOGEN

CeGaT

SONOGEN XP report for Richard Roe - Brief version

First name:	Richard	**Laboratory patient ID:**	999999
Last name:	Roe	**Report date:**	February 2, 2024
Date of birth:	March 1, 1985		
Gender:	male		

Pharmacogenetic profile

Gene	Genotype	Predicted phenotype/haplotype	Effect
CYP2C9	*1/*2	IM*2	intermediate (slower) metabolism
CYP2C19	*1/*17	RM	fast metabolism
CYP4F2	*1/*3	IM	intermediate (slower) metabolism
HLA-B	*15:02/*35:01	increased risk (*15:02)	high risk of adverse events
IFNL3	rs12979860-TT	unfavorable response	low response rate
SLCO1B1	*1/*5	decreased function	decreased drug efficacy
UGT1A1	*1/*28	IM	intermediate (slower) metabolism
VKORC1	-1639GA	decreased function	increased drug efficacy
ABCG2	421CC	normal function	normal drug efficacy
CACNA1S	WT/WT	normal risk	normal risk of adverse events
CYP2B6	*1/*1	NM	normal metabolism
CYP2D6	*1/*2	NM	normal metabolism
CYP3A4	*1/*1	NM	normal metabolism
CYP3A5	*3/*3	non-expresser	normal metabolism
DPYD	*1/*1	NM	normal metabolism
G6PD	B/B	normal	normal metabolism
HLA-A	*03:01/*24:02	normal risk	normal risk of adverse events
MT-RNR1	WT	normal risk	normal risk of adverse events
NUDT15	*1/*1	NM	normal risk of adverse events
POR	*1/*1	normal function	normal metabolism
RYR1	WT/WT	normal risk	normal risk of adverse events
TPMT	*1/*1	NM	normal metabolism

For HLA-A, the risk allele *31:01 was considered for phenotype classification.

Drug - PGx interactions of treatment - recommendations

	Normal risk	Use with caution	High risk
abacavir HLA-B normal risk (*57:01-negative)	• Use abacavir per standard dosing guidelines.		
abrocitinib CYP2C19 RM	• Follow drug label dosing recommendation.		
acenocoumarol VKORC1 decreased function	• Follow drug label dosing recommendation.		
allopurinol HLA-B normal risk (*58:01-negative)	• Follow drug label dosing recommendation.		
allopurinol ABCG2 normal function	• Follow drug label dosing recommendation.		
amikacin MT-RNR1 normal risk	• Follow drug label dosing recommendation.		
amitriptyline CYP2D6 NM, CYP2C19 RM		• High dose (e.g. depression): **Consider alternative drug not metabolized by CYP2C19** (e.g. nortriptyline, desipramine) If amitriptyline is warranted, utilize TDM to guide dose adjustment. • Low dose (e.g. neuropathic pain): Follow drug label dosing recommendation.	
aripiprazole CYP2D6 NM	• Follow drug label dosing recommendation.		
atazanavir UGT1A1 IM	• Follow drug label dosing recommendation.		
atomoxetine CYP2D6 NM		• **Start with 40 mg/day and increase to 80 mg/day after 3 days**. If no clinical response and in the absence of adverse events after 2 weeks, consider increasing dose to 100 mg/day to approach 400 ng/ml peak plasma concentration.	
atorvastatin SLCO1B1 decreased function			• **Use not more than 40 mg as a starting dose** and adjust doses based on disease-specific guidelines. • **Be alert to symptoms of myopathy,** especially with 40 mg atorvastatin. • If the patient has additional risk factors for statin-induced myopathy, **choose an alternative drug.** • **If dose over 40 mg is needed, consider combination therapy.**
azathioprine Normal thiopurine metabolism	• Follow drug label dosing recommendation.		
belinostat UGT1A1 IM	• Follow drug label dosing recommendation.		
brexpiprazole CYP2D6 NM	• Follow drug label dosing recommendation.		
brivaracetam CYP2C19 RM	• Follow drug label dosing recommendation.		
capecitabine DPYD NM	• Follow drug label dosing recommendation.		
carbamazepine HLA-A normal risk, HLA-B increased risk (*15:02)			• **Choose alternative treatment** in carbamazepine naïve patients. • **If patient has previously used carbamazepine for longer than 3 months without incidence of cutaneous adverse reactions, cautiously consider use of carbamazepine.**
carisoprodol CYP2C19 RM	• Follow drug label dosing recommendation.		
carvedilol CYP2D6 NM	• Follow drug label dosing recommendation.		

celecoxib CYP2C9 IM*2	• Follow drug label dosing recommendation.		
cevimeline CYP2D6 NM	• Follow drug label dosing recommendation.		
citalopram CYP2C19 RM		• Initiate therapy with recommended starting dose. • If patient does not adequately respond, **consider titrating to a higher dose or switching to an alternative** not predominantly metabolized by CYP2C19.	
clobazam CYP2C19 RM	• Follow drug label dosing recommendation.		
clomipramine CYP2D6 NM, CYP2C19 RM		• High dose (e.g., depression): **Consider alternative drug not metabolized by CYP2C19** (e.g. nortriptyline, desipramine). If clomipramine is warranted, utilize TDM to guide dose adjustment. • Low dose (e.g., neuropathic pain): Follow drug label dosing recommendation.	
clopidogrel CYP2C19 RM	• Follow drug label dosing recommendation.		
clozapine CYP2D6 NM	• Follow drug label dosing recommendation.		
codeine CYP2D6 NM	• Use label recommended age- or weight-specific dosing.		
dapsone G6PD normal	• Follow drug label dosing recommendation.		
desflurane Normal risk of MH	• RYR1 and CACNA1S phenotypes show no contraindication for the use of volatile anesthetics.		
desipramine CYP2D6 NM	• Follow drug label dosing recommendation.		
deutetrabenazine CYP2D6 NM	• Follow drug label dosing recommendation.		
dexlansoprazole CYP2C19 RM		• Initiate standard starting daily dose. • **Consider increasing dose by 50-100% for the treatment of H. pylori infection and erosive esophagitis**. Daily dose may be given in divided doses. • **Monitor for efficacy.**	
doxepin CYP2D6 NM, CYP2C19 RM		• High dose (e.g., depression): **Consider alternative drug not metabolized by CYP2C19** (e.g., nortriptyline, desipramine). If doxepin is warranted, utilize TDM to guide dose adjustment. • Low dose (e.g., neuropathic pain): Follow drug label dosing recommendation.	
efavirenz CYP2B6 NM	• Follow drug label dosing recommendation.		
eliglustat CYP2D6 NM	• Use the standard dose of 84 mg twice daily.		
escitalopram CYP2C19 RM		• Initiate therapy with recommended starting dose. • If patient does not adequately respond, **consider titrating to a higher dose or switching to an alternative** not predominantly metabolized by CYP2C19.	
fesoterodine CYP2D6 NM	• Follow drug label dosing recommendation.		
flecainide CYP2D6 NM	• Follow drug label dosing recommendation.		
flucloxacillin HLA-B normal risk (*57:01-negative)	• Follow drug label dosing recommendation.		
flucytosine DPYD NM	• Follow drug label dosing recommendation.		

fluorouracil DPYD NM	• Follow drug label dosing recommendation.		
flurbiprofen CYP2C9 IM*2	• Follow drug label dosing recommendation.		
fluvastatin CYP2C9 reduced metabolizer, SLCO1B1 decreased function		• **Use not more than 20mg as a starting dose** and adjust doses based on disease-specific guidelines. • **If dose >20mg needed for desired efficacy, consider an alternative statin or combination therapy.**	
fluvoxamine CYP2D6 NM	• Follow drug label dosing recommendation.		
gefitinib CYP2D6 NM	• Follow drug label dosing recommendation.		
gentamicin MT-RNR1 normal risk	• Follow drug label dosing recommendation.		
haloperidol CYP2D6 NM	• Follow drug label dosing recommendation.		
ibuprofen CYP2C9 IM*2	• Follow drug label dosing recommendation.		
iloperidone CYP2D6 NM	• Follow drug label dosing recommendation.		
imipramine CYP2D6 NM, CYP2C19 RM		• High dose (e.g. depression): **Consider alternative drug not metabolized by CYP2C19** (e.g. nortriptyline, desipramine). If imipramine is warranted, utilize TDM to guide dose adjustment. • Low dose (e.g. neuropathic pain): Follow drug label dosing recommendation.	
irinotecan UGT1A1 IM	• Follow drug label dosing recommendation.		
isoflurane Normal risk of MH	• RYR1 and CACNA1S phenotypes show no contraindication for the use of volatile anesthetics.		
lamotrigine HLA-B increased risk (*15:02)			• **Avoid lamotrigine if possible.** • **Carefully weigh the risk of SJS/TEN against the benefits.** • Carbamazepine is not an alternative, as the risk of SJS/TEN is higher. Oxcarbazebine and phenytoin have a similar risk of SJS/TEN. If it is not possible to avoid these products, advise the patient to **report any rash immediately.**
lansoprazole CYP2C19 RM		• Initiate standard starting daily dose. • **Consider increasing dose by 50-100%** for the treatment of H. pylori infection and erosive esophagitis. Daily dose may be given in divided doses. • **Monitor for efficacy.**	
lornoxicam CYP2C9 IM*2	• Follow drug label dosing recommendation.		
lovastatin SLCO1B1 decreased function			• **Prescribe an alternative statin** depending on the desired potency. • If lovastatin therapy is warranted, limit dose to 20 mg/day or less.
mavacamten CYP2C19 RM	• Follow drug label dosing recommendation.		
meloxicam CYP2C9 IM*2	• Follow drug label dosing recommendations.		
mercaptopurine Normal thiopurine metabolism	• Follow drug label dosing recommendation.		
metoprolol CYP2D6 NM	• Follow drug label dosing recommendation.		
nitrofurantoin G6PD normal	• Follow drug label dosing recommendation.		
nortriptyline CYP2D6 NM	• Follow drug label dosing recommendation.		

omeprazole CYP2C19 RM		• Initiate standard starting daily dose. • **Consider increasing dose by 50-100% for the treatment of H. pylori infection and erosive esophagitis.** Daily dose may be given in divided doses. • **Monitor for efficacy.**	
ondansetron CYP2D6 NM	• Follow drug label dosing recommendation.		
oxcarbazepine HLA-B increased risk (*15:02)			• **Choose alternative treatment** in oxcarbazepine naïve patients. • **If patient has previously used oxcarbazepine for longer than 3 months without incidence of cutaneous adverse reactions, cautiously consider use of oxcarbazepine.**
oxycodone CYP2D6 NM	• Follow drug label dosing recommendation.		
pantoprazole CYP2C19 RM		• Initiate standard starting daily dose. • **Consider increasing dose by 50-100%** for the treatment of H. pylori infection and erosive esophagitis. Daily dose may be given in divided doses. • **Monitor for efficacy.**	
paromomycin MT-RNR1 normal risk	• Follow drug label dosing recommendation.		
paroxetine CYP2D6 NM	• Follow drug label dosing recommendation.		
pazopanib UGT1A1 IM, HLA-B normal risk (*57:01-negative)	• Follow drug label dosing recommendation.		
peginterferon alfa-2a IFNL3-unfavorable-response genotype			• **Low response rates** in treatment naïve patients. • Approximately 60% chance for SVR after 24–48 weeks of treatment. Consider implications before initiating PEG-interferon-alfa and ribavirin - containing regimens.
peginterferon alfa-2b IFNL3-unfavorable-response genotype			• **Low response rates** in treatment naïve patients. • Approximately 60% chance for SVR after 24–48 weeks of treatment. Consider implications before initiating PEG-interferon-alfa and ribavirin - containing regimens.
perphenazine CYP2D6 NM	• Follow drug label dosing recommendation.		
phenprocoumon VKORC1 decreased function	• Follow drug label dosing recommendation.		
phenytoin HLA-B increased risk (*15:02)			• If patient is phenytoin-naïve, **do not use phenytoin**/fosphenytoin. • Avoid carbamazepine and oxcarbazepine.
pimozide CYP2D6 NM	• Follow drug label dosing recommendation.		
piroxicam CYP2C9 IM*2	• Follow drug label dosing recommendations.		
pitavastatin SLCO1B1 decreased function			• **Prescribe 2mg or less as a starting dose** and adjust doses based on disease-specific guidelines. • If dose >2mg needed for desired efficacy, consider an alternative statin or combination therapy. • **Be aware of possible increased risk for myopathy especially for doses >1mg.**
pitolisant CYP2D6 NM	• Follow drug label dosing recommendation.		
pravastatin SLCO1B1 decreased function			• Use desired starting dose and adjust doses based on disease-specific guidelines. • **Be aware of possible increased risk for myopathy especially with doses >40mg per day**.

primaquine G6PD normal	• Follow drug label dosing recommendation.		
propafenone CYP2D6 NM	• Follow drug label dosing recommendation.		
quetiapine CYP3A4 NM	• Follow drug label dosing recommendation.		
rasburicase G6PD normal	• Follow drug label dosing recommendation.		
ribavirin IFNL3-unfavorable-response genotype			• **Low response rates** in treatment naïve patients. • Approximately 30-60% chance for SVR after 24–48 weeks of treatment. Consider implications before initiating PEG-interferon-alfa and ribavirin-containing regimens.
risperidone CYP2D6 NM	• Follow drug label dosing recommendation.		
rosuvastatin Decreased transport activity		• Use desired starting dose and adjust doses based on disease-specific and specific population guidelines. • **Be aware of possible increased risk for myopathy** especially for doses over 20mg.	
sacituzumab govitecan UGT1A1 IM	• Follow drug label dosing recommendation.		
sertraline CYP2B6 NM, CYP2C19 RM	• Follow drug label dosing recommendation.		
sevoflurane Normal risk of MH	• RYR1 and CACNA1S phenotypes show no contraindication for the use of volatile anesthetics.		
simvastatin SLCO1B1 decreased function			• **Use an alternative statin.** • **If simvastatin is warranted, limit dose to 20 mg/day** and consider routine CK surveillance.
siponimod CYP2C9 IM*2	• Follow drug label dosing recommendation.		
streptomycin MT-RNR1 normal risk	• Follow drug label dosing recommendation.		
succinylcholine Normal risk of MH	• RYR1 and CACNA1S phenotypes show no contraindication for the use of succinylcholine.		
tacrolimus CYP3A5 non-expresser	• Initiate therapy with standard recommended dose. • **Use TDM to guide dose adjustments.**		
tamoxifen CYP2D6 NM		• Initiate therapy with recommended standard of care dosing (tamoxifen 20 mg/day). • **Avoid moderate and strong CYP2D6 inhibitors.**	
tenoxicam CYP2C9 IM*2	• Follow drug label dosing recommendations.		
tetrabenazine CYP2D6 NM	• Follow drug label dosing recommendation.		
thioridazine CYP2D6 NM	• Follow drug label dosing recommendation.		
tioguanine Normal thiopurine metabolism	• Follow drug label dosing recommendation.		
tobramycin MT-RNR1 normal risk	• Follow drug label dosing recommendation.		
tramadol CYP2D6 NM	• Follow drug label dosing recommendation.		
trimipramine CYP2D6 NM, CYP2C19 RM		• High dose (e.g. depression): **Consider alternative drug not metabolized by CYP2C19** (e.g. nortriptyline, desipramine). If trimipramine is warranted, utilize TDM to guide dose adjustment. • Low dose (e.g. neuropathic pain): Follow drug label dosing recommendation.	

tropisetron CYP2D6 NM	• Follow drug label dosing recommendation.		
venlafaxine CYP2D6 NM	• Follow drug label dosing recommendation.		
voriconazole CYP2C19 RM			• **Choose an alternative agent not mainly metabolized by CYP2C19** (e.g. isavuconazole, liposomal amphotericin B, and posaconazole)
vortioxetine CYP2D6 NM	• Follow drug label dosing recommendation.		
warfarin Intermediate warfarin sensitivity (incl. CYP4F2)		• **Calculate dose with a warfarin dose algorithm** (e.g. http://www.warfarindosing.org).	
zuclopenthixol CYP2D6 NM	• Follow drug label dosing recommendation.		

Predictable drug - PGx interactions

Table shows potential interactions of specific drugs with patient's PGx profile. These drugs are related to biomarkers, for which drug label recommendations or dosing guidelines exist, or for which LoE is at least C. For suggested action and detailed information, please indicate drug of interest in patient's treatment and refer to SONOGEN detailed report or consult drug labels or dosing guidelines.

Normal risk		Use with caution	High risk
abacavir (4)	lornoxicam (1)	amitriptyline (2)	atorvastatin (2)
abrocitinib (2)	mavacamten (1)	atomoxetine (2)	carbamazepine (4)
acenocoumarol (1)	meloxicam (2)	citalopram (2)	lamotrigine (1)
allopurinol (3)	mercaptopurine (3)	clomipramine (2)	lovastatin (1)
amikacin	metoprolol (1)	dexlansoprazole (2)	oxcarbazepine (3)
aripiprazole (2)	nitrofurantoin (2)	doxepin (2)	peginterferon alfa-2a (1)
atazanavir (1)	nortriptyline (2)	escitalopram (2)	peginterferon alfa-2b (2)
azathioprine (3)	ondansetron (1)	fluvastatin (1)	phenytoin (2)
belinostat (2)	oxycodone (2)	imipramine (2)	pitavastatin (2)
brexpiprazole (2)	paromomycin	lansoprazole (1)	pravastatin (1)
brivaracetam (2)	paroxetine (1)	omeprazole (2)	ribavirin (1)
capecitabine (3)	pazopanib (2)	pantoprazole (2)	simvastatin (3)
carisoprodol (2)	perphenazine (2)	rosuvastatin (2)	voriconazole (2)
carvedilol (2)	phenprocoumon (1)	tamoxifen (2)	
celecoxib (2)	pimozide (3)	trimipramine (2)	
cevimeline (2)	piroxicam (2)	warfarin (2)	
clobazam (2)	pitolisant (2)		
clopidogrel (2)	primaquine (4)		
clozapine (2)	propafenone (2)		
codeine (2)	quetiapine (1)		
dapsone (2)	rasburicase (4)		
desflurane	risperidone (1)		
desipramine (2)	sacituzumab govitecan (2)		
deutetrabenazine (2)	sertraline (1)		
efavirenz (2)	sevoflurane (2)		
eliglustat (4)	siponimod (4)		
fesoterodine (2)	streptomycin (1)		
flecainide (1)	succinylcholine (2)		
flucloxacillin (2)	tacrolimus (1)		
flucytosine (3)	tenoxicam (1)		
fluorouracil (3)	tetrabenazine (4)		
flurbiprofen (2)	thioridazine (2)		
fluvoxamine (2)	tioguanine (3)		
gefitinib (2)	tobramycin		
gentamicin (1)	tramadol (2)		
haloperidol (2)	tropisetron (1)		
ibuprofen (1)	venlafaxine (2)		
iloperidone (2)	vortioxetine (2)		
irinotecan (2)	zuclopenthixol (1)		
isoflurane			

() PGx information included in the drug label are classified by the Pharmacogenomics Knowledgebase (PharmGKB) into the following biomarker relevance categories: (4) required, (3) recommended, (2) actionable, (1) informative

Disclaimer

The present individual treatment optimization proposal and the related information was generated by SONOGEN XP - a clinical decision support and pharmacogenetic expert system. This software is an in vitro medical device and has been developed according to the directive on in vitro diagnostic medical devices (Directive 98/79/EC of the European Parliament and of the Council). The containing information has been collected and reviewed to our best knowledge, however there is no guarantee that it contains the latest scientific findings and that all adverse or important outcomes will be reported in the literature and integrated in the SONOGEN XP software. The responsibility for a correct drug-treatment prescription lies with the treating physician and the user should always apply his independent professional judgement.

Limitation

This pharmacogenetic test will not detect all the known mutations of a gene. Absence of a detectable gene mutation does not rule out the possibility of an altered phenotype due to the presence of an undetected mutation or due to other factors influencing the drug efficacy, such as drug-drug-interactions, comorbidities or lifestyle habits.

Legend

Biomarker Relevance (BR)

4	Genetic testing required. The drug label states that a genetic testing should be conducted before using this drug. This requirement may only be for a subset of patients. If the drug label states a test "should be" performed, this is to be interpreted as a requirement.
3	Genetic testing recommended. The drug label states that a genetic testing is recommended before using this drug. This recommendation may only be for a subset of patients. If the drug label states a test "should be considered", this is to be interpreted as a recommendation.
2	Actionable PGx. The drug label does not discuss testing for gene variants, but does contain information about changes in efficacy, dosage or toxicity (due to such variants). The drug label may mention contraindication of the drug in a subset of patients but does not require or recommend genetic testing.
1	Informative PGx. The drug label mentions a gene/protein is involved in the metabolism or pharmacodynamics of the drug but gives no information to suggest that variation in this gene/protein leads to a different response.

Level of Evidence (LoE)

E	The variant-drug combination is based on published incomplete case reports, non-significant studies or in vitro, molecular or functional assay evidence only.
D	The variant-drug combination is based on published case reports, well documented, and having relevant pharmacokinetic or clinical endpoints.
C	The variant-drug combination shows moderate evidence of an association (it is replicated but there may be some studies that do not show statistical significance, and/or the effect size may be small). Or drug label information on PGx relevant genes with potential influence on pharmacokinetics, without information on specific variants.
B	The variant-drug combination shows good evidence of an association (it is replicated in more than one cohort with significant p-values, and preferably will have a strong effect size). Or drug label information on specific variants of PGx relevant genes with potential influence on pharmacokinetics. Or the variant-drug combination and recommendation are reflected in peer reviewed articles.
A	The variant-drug combination is reflected in a pharmacogenetic guideline (e.g. CPIC, DPWG), or implemented at a pharmacogenomic research network site (e.g. www.warfarindosing.org) or in another major health system. Or FDA box warning. Or drug label recommendation on pharmacogenetic testing or dosing for specific genotype/phenotype.

PGx - Phenotype

APS	average pain sensitivity
HPS	high pain sensitivity
IA	intermediate acetylator
IM	intermediate metabolizer
IM+	intermediate metabolizer with higher enzyme activity than IM
IM*2	IM with one *2 allele or equivalent (*8, *11, *12)
IM*3	IM with one *3 allele or equivalent (*4, *5, *6, *13, *14, *15, *25)
LPS	low pain sensitivity
NM	normal metabolizer
PM	poor metabolizer
PM+	poor metabolizer with higher enzyme activity than PM

PM*2	PM with two *2 alleles or equivalent (*8, *11, *12)
PM*3	PM with two *3 alleles or equivalent (*4, *5, *6, *13, *14, *15, *25)
PM*2/*3	PM with one *2 allele or equivalent (*8, *11, *12) and one *3 allele or equivalent (*4, *5, *6, *13, *14, *15, *25)
RA	rapid acetylator
RM	rapid metabolizer
SA	slow acetylator
UM	ultrarapid metabolizer

For further information, please refer to the detailed report.

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